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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,942	05/04/2005	Enrico Garaci	725.1046	9693

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EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
1628	

NOTIFICATION DATE	DELIVERY MODE
10/14/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@lmiplaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/533,942	GARACI ET AL.	
	Examiner	Art Unit	
	Paul Zarek	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-9 and 13-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-9 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 13-18 have been added by the Applicant in correspondence filed on 06/23/2009. Claims 4-9 and 13-18 are currently pending. This is the second Office Action on the merits of the claim(s) following a request for continued examination.

RESPONSE TO ARGUMENTS

2. Claims 4-9 were rejected under 35 U.S.C. 103(a) as being unpatentable over Root, et al. (Journal of General Virology, 2000), in view of Stewart, et al. (Biochemistry, 1999), and Heredia, et al. (Journal of Acquired Immune Deficiency Syndromes, 2000). Applicants traversed this rejection on the grounds that the combination of Root, et al., Stewart, et al., and Heredia, et al., do not teach or fairly suggest the claimed invention. Specifically, Applicants assert that Root, et al., teach that only a specific PKC inhibitor (bisindolylmaleimide 1.HCl) is capable of inhibiting influenza virus entry into target cells, that other PKC inhibitors, such as H7, have no effect on influenza virus entry, and that the disclosed PKC inhibitor reversibly inhibits viral entry. Applicants further assert that Root, et al., teach that not all viruses behave in the same fashion and that this prior art does not teach or suggest resveratrol as a PKC inhibitor. Applicants contend that Stewart, et al., teach that the anti-cancer activity of resveratrol cannot be based on its PKC inhibitory activity because resveratrol is a weak PKC inhibitor such that an effective dose of resveratrol would be highly toxic to mammalian cells. Moreover, Applicants contend that Stewart, et al., teach that resveratrol inhibits a broad spectrum of protein kinases,

indicating that resveratrol is not a specific PKC inhibitor. Applicants state that Heredia, et al., does not teach or suggest the instant invention because Heredia, et al., are concerned with HIV, not influenza, and that the art worker would not find motivation within Heredia, et al., to use resveratrol for the treatment of influenza. Examiner respectfully disagrees.

3. "Influenza virus replication" is not defined in the instant claims or the specification. Thus, one of ordinary skill in the art would reasonably interpret "influenza virus replication" to encompass any disruption of the viral life cycle, such as inhibiting entry into a target cell. If a virus cannot enter a target cell, the virus can not replicate, and, thus, influenza virus replication is inhibited. Furthermore, Examiner notes that instant Claims 7-9 do not claim a method of inhibiting influenza virus replication; rather, they are drawn to a method of treating an influenza virus infection. As such, inhibiting entry of the influenza virus into a target cell is a treatment of influenza virus infection.

4. Root, et al., explicitly teach bisindolylmaleimide 1.HCl inhibits viral replication in a dose-dependent manner, and that PKC is crucial for influenza virus entry and may be a target for antiviral therapy (pg 2698, paragraph spanning cols 1 and 2). That bisindolylmaleimide 1.HCl inhibits entry of the influenza cell into target cells in a reversible manner is not relevant because is nothing in Claims 4-9 that require a specific type (reversible or irreversible) of PKC inhibition. "Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993) (MPEP §2145(VI)). Root, et al., discuss the apparent contradictory nature of one PKC inhibitor inhibiting cell entry (bisindolylmaleimide 1.HCl) but another (H7) not inhibiting entry. Root, et al., teach that H7 and staurosporine are "nonselective in their action

and inhibit a wide range of different protein kinases" (pg 2698, col 1, para 4, lines 5-8). The inability of H7 and staurosporine to inhibit virus entry into the cell is due to the nonspecificity of these compounds, not PKC inhibition. Applicants' argument that different viruses respond differently to PKC inhibition is not persuasive because Root, et al., specifically demonstrate the importance of PKC inhibition on the influenza virus, the virus specified in the instant claims. Thus, Root, et al., demonstrate the ability of a PKC-specific inhibitor to inhibit cellular entry of the influenza virus, which would both inhibit viral replication and treat influenza virus infection. Root, et al., do not discuss resveratrol for the inhibition of influenza virus cell entry or treating influenza virus infection.

5. Examiner respectfully disagrees with Applicants' interpretation of Stewart, et al., with respect to the ability of resveratrol to inhibit PKC. The passages of Stewart, et al., which Applicants cite indicating that resveratrol is a weak PKC inhibitor do not support Applicants' conclusion. Stewart, et al., teach that resveratrol "potently inhibits" cellular PKC at a concentration of 15 μM (pg 13249, col 2, para 1, lines 4-5). Stewart, et al., teach that resveratrol is "weakly inhibitory" against a broad spectrum of protein kinases related to PKC (i.e. Lck) and that toxic doses of resveratrol are required to exert a chemopreventative effect against cancers (pg 13249, col 2, para 2). Stewart, et al., do not discuss the role of PKC or resveratrol on influenza virus. Thus, Stewart, et al., provides only that resveratrol inhibits PKC. Taken together, Root, et al., and Stewart, et al., teach that resveratrol, by inhibiting PKC, would be an effective inhibitor of influenza virus replication (by inhibiting viral entry into the target cell) and treatment for influenza virus infection. Neither Root, et al., nor Stewart, et al., provide a

motivation to utilize resveratrol over another PKC inhibitor (i.e. bisindolylmaleiminde 1.HCl) for such inhibition/treatment.

6. Heredia, et al., explicitly teach the virtues of resveratrol (i.e. low cost, established safety profile). The skilled artisan would be motivated to use naturally occurring resveratrol because it is already generally regarded as safe and relatively easy and inexpensively obtained. That Heredia, et al., discusses the ability of resveratrol to treat HIV does not negate the stated advantages with respect to drug development. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use resveratrol to inhibit influenza virus replication or treat influenza virus infection. The rejection of Claims 4-9 under 35 U.S.C. 103(a) as being unpatentable over Root, et al., in view of Stewart, et al., and Heredia, et al., is maintained.

7. Newly added Claims 13-18 are examined on their merits and the following **FINAL** rejection is made.

Claim Objections

8. Claims 13 and 16 are objected to because of the following informalities: These claims contain the word "non-reversably," which is misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 103

9. The text of Title 35, U.S.C. § 103(a) can be found in a prior Office action.

10. Claims 13-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Root, et al. (above), in view of Stewart, et al. (above), and Heredia, et al. (above).

11. Claims 13-15 are drawn to a method of non-reversibly inhibiting influenza virus replication comprising administration of resveratrol to a subject having an influenza infection. Claims 16-18 are drawn to a method of treating an influenza virus infection comprising administration of resveratrol whereby said virus is non-reversibly inhibited. Claims 14 and 17 limit the subject to human. Claims 15 and 18 limit the subject to a veterinary animal. The "whereby" clause of Claim 16 is considered the intended result of resveratrol administration. The intended result of a method is not considered to be a patentably distinguishing feature of an invention. "[A] whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'" *Hoffer v. Microsoft Corp.*, 405 F.3d 1326, 1329, 74 USPQ2d 1481, 1483 (Fed. Cir. 2005) (MPEP § 2111.04)

12. Root, et al., Stewart, et al., and Heredia, et al., were discussed above. Briefly, Root, et al., teach that influenza virus replication is reversibly inhibited by the specific PKC inhibitor bisindolylmaleimide 1.HCl. Stewart, et al., teach that resveratrol inhibits cellular PKC at a concentration of 15 μM. Heredia, et al., provide a motivation to use resveratrol (i.e. low cost and established safety profile). The intended result of Claims 16-18 (non-reversibly inhibiting influenza virus replication) is not considered patentably distinguishing limitations. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to treat influenza virus infection in a human or veterinary animal comprising the administration of resveratrol.

13. Claims 13-15 are drawn to the non-reversible inhibition of influenza virus replication. Although Root, et al., disclose only a reversible PKC inhibitor, one of ordinary skill in the art would be motivated to use any PKC inhibitor, regardless of whether it was reversible non-reversible. The motivation to use resveratrol lies in its disclosed ability to inhibit PKC (Stewart, et al.) and its desirably cost and safety profile (Heredia, et al.). That Applicants discovered that resveratrol is a non-reversible inhibitor of PKC does not render the claimed invention nonobvious over the prior art. "Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979)" (MPEP § 2145(II)). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use resveratrol to non-reversibly inhibit influenza virus replication.

Conclusion

14. Claims 4-9 remain rejected. Claims 13-18 are rejected.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brendon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/San-ming Hui/
Primary Examiner, Art Unit 1628